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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/844,268 | 07/25/2001 | Brad T. Bosworth | 21419/91513 | 9905 |

23644 7590 03/22/2004

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| EXAMINER | |
|---|---|
| WOITACH, JOSEPH T | |
| **ART UNIT** | **PAPER NUMBER** |
| 1632 | 10 |

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/844,268 | BOSWORTH ET AL. | |
| | Examiner | Art Unit | |
| | Joseph T. Woitach | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2,4 and 6-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4 and 6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

This application filed April 27, 2001 is a continuation of 09/443,766 filed November 19, 1999, which claims benefit under 35 U.S.C. 120 to PCT/US98/10318, filed May 20, 1998, which claims benefit to provisional application 60/047,181, filed May 20, 1997.

The preliminary amendment filed July 18, 2001, paper number 7, has been received but not entered. The amendments to the specification indicated in the preliminary amendment could not be entered because they were not consistent with the specification in the file. The amendment has been placed in the file but not entered. Applicants amendment filed June 27, 2003, paper number 9, has been received and entered. The specification has been amended. Claims 1, 3 and 5 have been canceled. Claims 8-11 have been added. Claims 2, 4 and 6-11 are pending and currently under examination.

### *Information Disclosure Statement*

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specifically, on page 20, a listing of references cited has been set forth, however no copy of the references have been provided, nor has an IDS been filed.

### *Oath/Declaration*

It is noted that copies of two separate declarations have been filed and are present in the file. Consistent with the declarations filed in 09/443,766, one copy contains alterations which have not been initialed. The substitute declarations that were subsequently filed June 28, 2001, are in compliance with 37 CFR 1.67.

### *Claim Objections*

Claim 10 is objected to because of the following informalities: position is misspelled "posiiton".

Appropriate correction is required.

### *Claim Rejections - 35 U.S.C. § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". In the instant case the product set forth in claim 11 is considered new matter. Initially it is noted that Applicants have not pointed to support for the amendment. Upon review of the specification, literal support for the enzymes can be found in the working examples, however there is no support in the specification of the art of record that these are use to amplify sequences of FUT1. Further, since the literal support for the enzymes are present in a working example there is no support that it was contemplated for use with sequences other than those from swine or that such enzyme consensus sequences exist in FUT1 genes from other species. Finally, the enzymes were used in a specific assay separate from the disclosed invention, and it does not appear that the specification teaches that the assay should be developed into a method of producing a product nor does it appear that the specification contemplates any specific use of any fragment generated in said assay.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claim 11 is also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure" (emphasis added).

Claims 2, 4, 6-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the

'written description' inquiry, *whatever is now claimed.*" *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, while the specific SEQ ID NO: 12 and the specific sequence at position 307 are adequately set forth, outside these specific sequences lacks written description. It is noted that the specification contemplates other sequences and use thereof however the specification fails to provide any description or clear guidance to what these genes would be, and more specifically, what sequences are comprised within these claims. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). The specification teaches that it was observed that certain swine were resistant to intestinal disorders, in particular they were resistant to problems associated with *E. coli* colonization. The specification demonstrates that the presence of the homozygous FUT1 allele represented by an adenine at position 307 of the open reading of FUT1 is associated with resistance to *E. coli* strain F18 associated intestinal disorders. Importantly, the specification only provides only this single specific alteration in the FUT1 allele

and its association with only *E. coli* strain F18. It may be that other strains of *E. coli* strains can cause intestinal disease associated with colonization, however as noted by Bertin *et al.* and Duchet-Suchaux *et al.*, resistance of a swine to one strain of *E. coli* does not indicate resistance to other strains of *E. coli.* Thus, the presence of resistance to one strain of *E. coli*, is not, *a priori*, predictive of resistance to other strains of *E. coli.* In this case the basis for the observed resistance in swine associated with the specific alteration in the FUT1 allele is not known. Absent evidence that the polymorphism results in a mechanistic reason for the resulting resistance, a genetic marker/polymorphism is simply a marker which can be associated with a specific characteristic. For example, the specification defines several other polymorphism in coding regions of the FUT1 and FUT2 genes, however none of these polymorphism are associated with any resistance to *E. coli* or any other observable phenotype. There is no evidence that the polymorphism itself results in the phenotype, therefore the adenine at position 307 of the open reading of FUT1 gene represents only a marker for the phenotypic observation of a swine resistance to F18 *E. coli.* In the instant case, Applicants have shown a correlation with the presence of a homozygous polymorphism at base 307 in the open reading frame of the FUT1 gene and a resistance to F18 and thus, absence of the associated diseases. However, the mechanism of this resistance is not known nor described. Even post filing art, Merjerink *et al.* (Mammalian Genomics 8:736-741), including one of the inventors-Vogeli, clearly indicates that the mechanism of the resistance was unknown at the time of the claimed invention (summarized in final sentence of abstract). Therefore, at the time of the invention made, the observation of the

polymorphism associated with F18 resistance represents only a correlative analysis linking a specific phenotype with a specific polymorphism and would not necessarily be extended to resistance to other strains of *E. coli*. In the instant case, the specification asserts that other sequences exist however there is no disclosure of these sequences and fails to describe the relevant identifying characteristics of any of the nucleic acid sequences of any of the genes and sequences of the instantly claimed products. The skilled artisan cannot envision all the possible sequences encompassed by the claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Applicants attention is drawn to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein it was stated:

In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not

suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers,* 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. *See In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provides only SEQ ID NO: 12 and the alteration at position 307, thus the rejected claim fails to meet the written description requirement under 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 4, 6-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 2 is unclear in the recitation of "in SEQ ID NO: 12" because it is not clear if the sequence being claimed is SEQ ID NO: 12 in which at position 307 is adenine or whether the

claim is drawn to any poly nucleotide in which position 307 is an adenine. It is unclear if the product claimed must comprise SEQ ID NO: 12 or if it is provided as a general reference. More clearly setting forth the specific isolated DNA molecule being claimed in relationship to SEQ ID NO: 12 would obviate the basis of the rejection. Dependent claims 4, 6, and 7 are included in the basis of the rejection because they do not further clarify the basis of the rejection in that they are drawn to complementary or smaller fragments of claim 2 which is unclear.

Claims 8 and 9 are vague and unclear in the recitation of the metes and bounds of the probe. It is unclear if the probe must directly detect the particular sequence indicated or if it encompasses identification by other means and thus encompasses probes outside the specific sequence and even primers of a plasmid which can be used to sequence a PCR fragment of the FUT1 gene. The claims are indefinite because it is not clear if the limitation of detecting is physical or functional attribute of the probe being claimed.

Claim 10 is indefinite because the mete and bounds of what can be included is not clearly set forth. Initially, it is unclear what the claim includes if the genome does not have the particular polymorphism. Further, it is unclear what the metes and bounds of what would be considered in disequilibrium because this is a relative term and subject to change depending on how it is evaluated and determined.

Claim 11 is unclear and confusing because restriction enzymes CfoI and ACiI can not produce amplified fragments. It appears that the claim attempts to encompass products made by a particular process, however there are no method steps set forth to distinguish any potential

product or any clear link to how restriction enzymes generate amplified fragments. Moreover, the claim does not even set forth the nature encompassed by "fragments" i.e. RNA, cDNA, genomic DNA, protein,...

***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 2, 4, 6-10 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The instant application and US Patent 6,355,859 share one common inventor and no common assignee. Each specification discloses that an adenine at position 307 of the open reading frame of the FUT1 gene is associated with resistance to F18 *E. coli* in swine. In addition, each application teaches that the artisan can use this association of F18 *E. coli* resistance for identification and possible treatment of swine suffering from effects of *E. coli* colonization. Importantly, the instantly claimed polynucleotides are required to practice the invention in '859. In light of the very similar teachings and claims in each application, the contribution of the different inventive entity for each application is unclear. Clarification of each Inventors contribution to the instant invention, and/or amendment of inventorships is required.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 3 and 4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,355,859. Although the conflicting claims are not identical, they are not patentably distinct from each other.

In the instant application, claims are drawn to a method for identifying a swine that is resistant to intestinal colonization to a of strain of *E. coli* associated intestinal disorders by determining whether base pair 307 of the open reading frame of FUT1 is an adenine, and in particular the *E. coli* is strain ECF18R. In '859 claim 4, which dependent on claim 1, is drawn to a method for controlling weight in a swine by determining whether a swine is genetically resistant to F18 *E. coli* colonization by determining base pair 307 of the open reading frame of FUT1 is an adenine. It is well known in the art that colonization of specific strains of *E. coli*,

such as F18, result in severe diarrhea and result in weight loss. Practicing the method encompassed by claims 3 and 4 in the instant application results in identifying a swine which is resistant to F18 *E. coli* colonization and the resulting symptoms associated with said colonization and therefore, would make obvious the identification a swine capable of more controlled weight gain in a herd generally susceptible to F18 *E. coli* colonization. Practicing the method encompassed by claims 3 and 4 of the instant specification would anticipate the method and results accomplished in claims 1 and 4 in '859.

Claims 3-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,596,923. Although the conflicting claims are not identical, they are not patentably distinct from each other.

In this case the method of '923 would anticipate the instantly claimed methods set forth in claims 3 and 4 because in each case a alteration/mutation if the FUT1 gene is being identified. Moreover, the mutation/alteration in the FUT1 gene is associated with decreased intestinal disorders. Claim 5 comprises practicing the methods set forth in claims 3 and 4 and provides an additional step of mating the identified swine for the implicit intention of obtaining additional or more pure bread swine with the particular genotype that is associated with the desired phenotype of being more resistant to intestinal disorders associated with *E. coli*. Claim 6 specifically sets forth that the *E. coli* is strain F18, which is specifically set forth in claim 1 of '923. Claims 5 and

6 are included in this rejection because they would be considered an obvious step of practicing the method set forth in claim 1 (also of claims 3 and 4) as set forth in step (a) of claim 5.

***Conclusion***

No claim is allowed. The claims are free of the art of record. The art indicates that cell surface receptors on intestinal cells are the target molecules for *E. coli* colonization, and that the glycosylation on said receptors may be important in determining the ability of a particular *E. coli* to colonize the intestine. However, the art fails to specifically teach that an adenine at position 307 of the open reading frame of alpha (1,2) fucosyltransferase (FUT1) (SEQ ID NO: 12) can be correlated with resistance to *E. coli* strain F18 and possibly with the subsequent associated diseases.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

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